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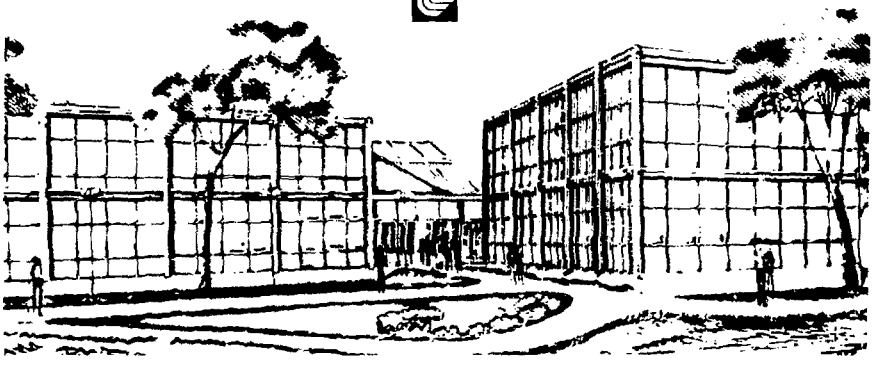

AUTOMATED SAMPLE CHANGER FOR X-RAY FLUORESCENCE ANALYSIS OF BIO-MEDICAL SAMPLES*

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INTRODUCTION

The first demonstration of a clinically useful application of fluorescent excitation analysis (FEA) was that of thyroid imaging (1). A collimated source of Am-241 was scanned across a thyroid gland, thus fluorescing the naturally occurring iodine within the gland. A Si(Li) detector mounted in close proximity to the source recorded iodine x rays which resulted in an image of the iodine distribution. Later, quantitation of the iodine content of the thyroid was shown to be of clinical significance (2,3).

Another successful application of FEA in medical work has involved in-vivo and in-vitro quantitation of purposefully administered stable tracers (4). For reasons discussed elsewhere in these Proceedings (5), in-vitro techniques are particularly useful, both in their application

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and acceptance. The number of clinically significant uses of FEA and the number of samples being analyzed have been increasing; therefore, the need for an automated sample changer adapted to the requirements imposed became apparent over a year ago. To date, commercial sample changers have been developed around the concept of turntables which accept circular samples or 35 mm slide-mounted samples. A sample changer useful for in-vitro techniques has substantially different requirements, including the following:

- Preserve the desired 90-deg geometry between exciting and fluorescencing beams.
- Automatically change and count a preset number of samples.
- Incorporate a mixing capability for liquid samples such as heparinized whole blood which will settle relatively quickly.
- Incorporate the inexpensive and disposable 2-cc vials already in use, if possible.
- Operate in a manual or automatic mode, single or multiple cycle.
- Allow for easy interchange of Am-241, Cd-109 or other useful excitation sources.

In addition to these features, there were the standard requirements of simple and easy operation by medical technicians and reasonable cost for the changer. In the following sections, the changer's basic components and operation are described; the more important mechanical features are presented; and finally, a brief description is given of the basic electronic logic used for control.

DESCRIPTION OF THE CHANGER

Two views of the sample changer with the detector housing and cryostat removed are shown in Figs. 1 and 2. In Fig. 1, two of the 35-cm-diameter sample trays are shown; the left one is in position for counting, while the right one rests on top of a swing-out graded shield (12.5-mm aluminum, 3.1-mm lead, 1.6-mm cadmium, 0.8-mm copper, and 0.8-mm aluminum, anodized). This shield is needed because FEA results are often compared to results from simultaneous radio-tracer studies.

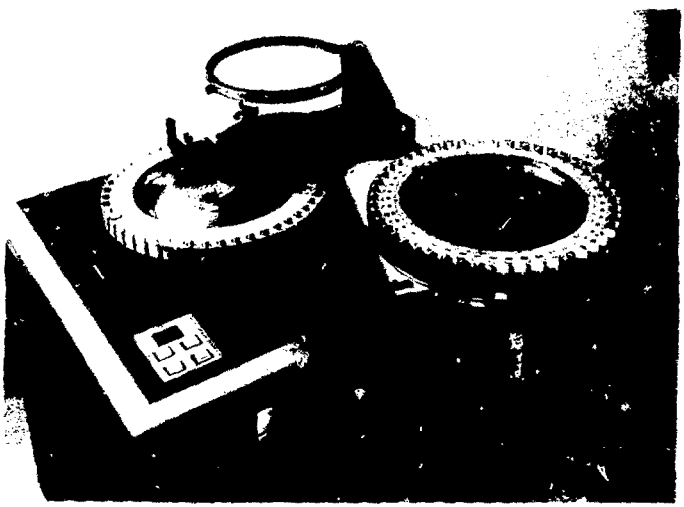

Fig. 1. Sample changer without Si(Li) detector, cryostat, and radiation exciter. The lefthand tray is in proper position for counting; the sample holder is down.

The sample trays are stackable and have a capacity of 48 2-cc vials. The vials are inexpensive and disposable.

The sample lift mechanism shown in the left foreground of Fig. 1 consists of an almost closed loop which when raised encircles and captures the sample vials. Within the tray the vials are supported by a small, raised, round platform at the end of a slim radial arm extending from the inside edge of the ring-shaped tray. This platform is easily seen in Fig. 3. A circular, recessed indentation in the bottom of the vial aids in self-centering the vials when they are returned to the tray. Shortly after the vials are captured by the nearly closed loop, an accessory arm gently presses down on the top of the vial to positively

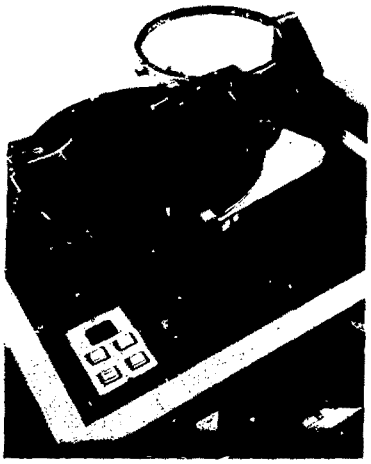

Fig. 2. Sample changer with graded shield closed and sample in proper position for counting. Detector, cryostat, and radiation exciter have been removed.

hold it in place. The accessory arm prevents loss of th vial during an optional MIX mode. Figures 1 and 2 show the sample lift mechanism in its lower and upper positions, without and with a sample. The unique four-right-angle configuration of the vial holder prevents the exciting radiation from scattering from or exciting the metal.

The MIX mode is necessary because whole blood settles during the period prior to assay. Without mixing, concentration determinations cease to be representative of tracer concentrations in the sample. If the MIX mode is selected by means of the MIX switch on the primary control panel (Fig. 4), the 2-cc vial will be tumbled end-over-end four times during the last 10 cm of travel (2.5 cm/s). Three times is sufficient to completely mix heparinized blood which has settled for 24 hours. At the end of lift, the sample is located at the intersection of the collimated source radiation beam and detector collimation. These lower and upper positions are shown from another perspective in Fig. 5. This is a double exposure – the first taken with the sample holder down, the second with the sample captured and positioned in front of the source and detector.

The changer may be operated either in a manual or automatic mode (Fig. 4). In the manual mode, sample advance, load and unload are activated by means of single-action push button switches located on the secondary control panel, a triple width Nim bin module shown in Fig. 6. In the manual mode the associated multichannel analyzer is operated in the traditional fashion in order to accumulate data. In the automatic mode the changer is controlled by pre-programmed software loaded in the

Fig. 3. Magnified view of three vial slots in the sample tray. Note the raised circular platform which is similar in shape to an indentation in the bottom of the 2-cc sample vials used.

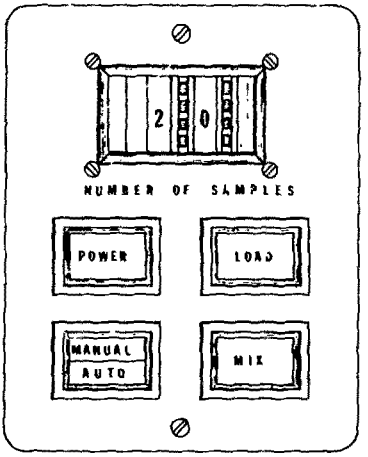

Fig. 4. Lighted push button controls on the primary control panel of the sample changer.

analyzer and appropriate data entered via the teletypewriter. When the automatic mode is selected, generally the number of samples to be analyzed – up to 48 – is first entered on the digital selection switch on the primary control panel. Then the sample turntable is set to the "home" position (Sample 1), and the MIX or non-MIX (MIX light off) mode is chosen.

The initial counting cycle begins immediately after the LOAD switch on the primary control panel is depressed. This initiates the sample lift mechanism and also loads the number of samples, n, into a counter. When sample lift is completed, a logic signal is sent to the analyzer and data accumulation begins for a pre-set time or number of counts. When data accumulation ends, pre-loaded software carries out appropriate spectral region integrations, background subtraction, and calibrations with the elemental concentrations (in mg/g or mEq/l) printed out by the teletype. After data output, the analyzer returns a logic pulse to the changer which initiates "unloading," i.e. returns a sample to the tray. The sample turntable then automatically advances to the next sample

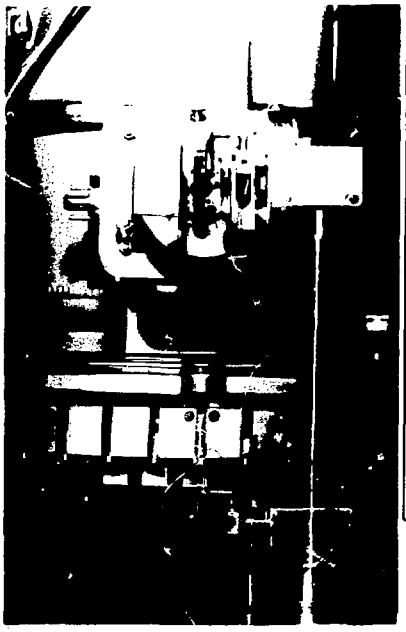

Fig. 5. A double exposure showing the sample holder in the down position (no sample captured), and in the raised position (sample captured).

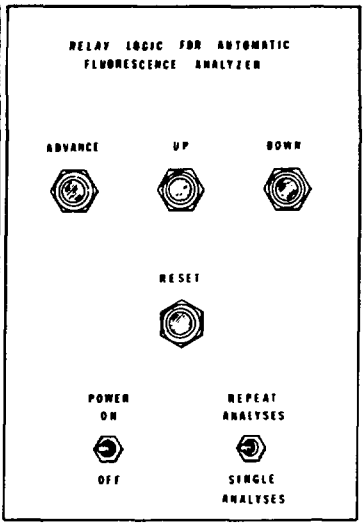

Fig. 6. Push button and toggle switch controls on the secondary control panel (*triple width Nim-bin*). This panel provides for control of the sample when the changer is in the MANUAL mode.

position. This loading, analyzing, and unloading cycle continues through the number of samples entered via the digital selection switch (the counter counts down to zero). Following analysis and unloading of the last sample, the changer will advance to its "home" position. At this point a switch on the secondary control panel allows for either SINGLE or REPEAT analysis of the group of n samples.

MECHANICAL DRIVE MECHANISMS

The sample changer contains three motorized subassemblies, each driven by small Bodine double-gear reduction motors with fixed-torque slip clutches. The first of these is shown at the top of Fig. 7 and labeled M1 (40 rpm). It drives the turntable through a Geneva-type intermittent motion. When M1 is turned off, a dynamic brake will stop the turntable at an indexed position to within ±0.25 mm. One complete revolution of the turntable (48 sample positions) requires 36 seconds. The "home" position is sensed by a microswitch which is operated by the cam seen in Fig. 7. In the event the turntable jams, the clutch in M1 slips and continues to slip until the jam condition is removed. No reset or retiming is necessary once the jam is cleared. Two additional microswitches (not visible) sense when the turntable is in a proper indexed position and turn M1 off.

The sample is raised 18.9 cm by a ball screw shaft which is driven by motor M2 (52 rpm) and is shown in Fig. 8. The microswitch seen above S5 governs the lift height. Its location on the stationary lift rod seen in Fig. 8 is adjustable. When this microswitch is tripped an electric clutch-brake unit, shown between S6 and M2, stops M2 within ±0.25 mm so that sample height is accurately maintained. Reversal of M2 lowers the sample, and when a microswitch located near the bottom of the rod is tripped the clutch-brake again stops M2. Figure 8 shows the lift mechanism in the sample down position. Note the contact between the adjustable screw and the lower microswitch. A safety slip clutch shuts off power to the entire changer unit in the event a jam occurs either during sample lift or lowering. This is to prevent or minimize damage to the sample lift arm. A flip-out pin in the clutch must be manually reset before power to the changer can be restored.

Motor M3 (40 rpm) controls the mixer drive subassembly. When the lift mechanism raises the sample, subassembly M3 moves up as a result of a coupling to the right shaft or tube, as shown in Fig. 8. When fixed microswitch S5 senses a depression (cam) in the moving subassembly, M3 is turned on. The pause allows the sample to clear the turntable and shield cover (about 9 cm of travel) before the mixing action starts. A four-position Geneva mechanism is used to turn the large gear at the bottom of the M3 subassembly. Through the Geneva gear and a 1-to-4 gear system, M3 rotates a long vertical shaft which is coaxially contained within the rightmost tube of Fig. 8. The inner shaft terminates inside of the small mixing head unit shown in Fig. 2. Within this unit

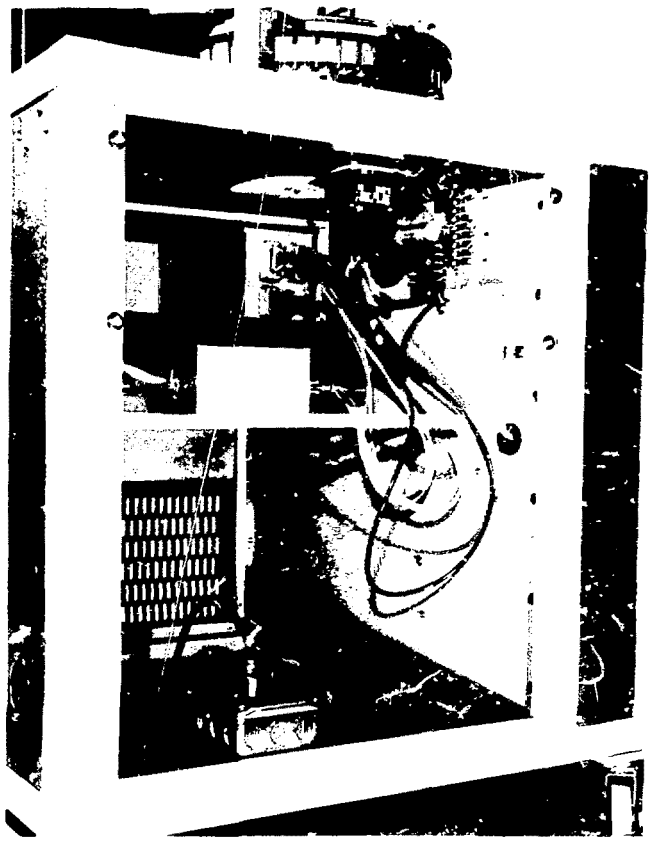

Fig. 7. Rear of the sample changer (panel removed) showing motor M1 which advances the sample tray.

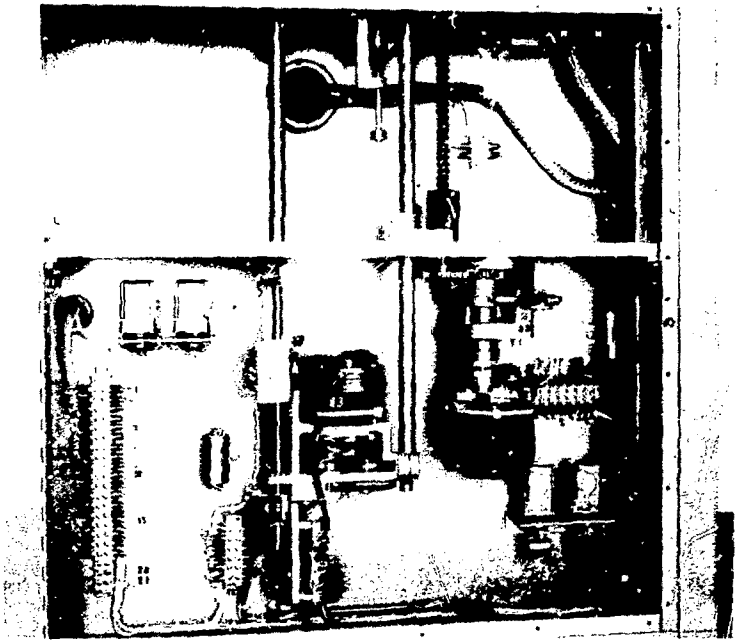

Fig. 8. One side of the sample changer (110V AC interlock door open) showing the motors M2 and M3 which control the lifting and mixing motions of the sample.

a right-angle drive converts vertical to horizontal rotary motion. The sample located at the end of a small arm (see Figs. 1 and 2) is therefore flipped end-over-end four times. The Geneva gear also creates a flip action followed by a short dwell rather than a continuous end-over-end motion. The flip-dwell motion results in a more desirable mixing action than a slow continuous turn.

Since the sample is captured by an open loop and then flipped, it is necessary to positively clamp the sample vial in position during the mixing action. The small wire clamp (visible in Figs. 1 and 2) is partly controlled by the spring-loaded rod shown in the upper center portion of Fig. 8. Through mechanical design coupled with the compressed spring, the clamp automatically pauses during the first 3 cm of lift, then moves down to clamp the captured vial in place. The clamp has an adjustable tension controlled in the lifting head. Only the clamp action is reversed when the sample is lowered; the flipping action does not occur during sample return to the tray.

The motor subassemblies shown in Fig. 3 were photographed with an access door open. An interlock on this door causes shutdown of changer power in the event the door is opened. Once the door is closed, a RESET switch on the secondary (Nim-bin) control panel must be depressed to regain power to the changer.

In summary, the three motors M1, M2 and M3 are off when the sample is in position for fluorescence. After a sample is returned to the turntable, M2 and M3 are off and M1 is on only during turntable rotation.

ELECTRONIC LOGIC

The electronic control logic of the changer consists of three major control areas: the control logic, the relay logic, and the motor wiring logic. The control logic is contained in a double-width Nim-bin and consists of transistor-to-transistor logic (TTL) integrated circuits that keep track of the sample count and route or receive control signals in the proper sequence via relays to the three motors.

The relay logic is contained in a triple-width Nim-bin. Eleven relays are contained in this bin with four others housed in the mechanical motor section (Fig. 8). This triple-width module also contains the single-step control circuitry used in the MANUAL mode. When this mode is chosen, all power to any AUTO mode controls are bypassed. The front panel of this three-width module, i.e. the secondary control panel, is shown in Fig. 6. This module also contains the interface circuitry from the 110-V ac required for motor control to the 5 V required for TTL logic. Electronic white noise generated by closure of various relay contacts created serious problems in the control logic even when extensive shielding was used. It was only after installation of separate filters on each logic and voltage line between the relay and the control

logic that all interference was eliminated (the rectangular box seen in Fig. 7).

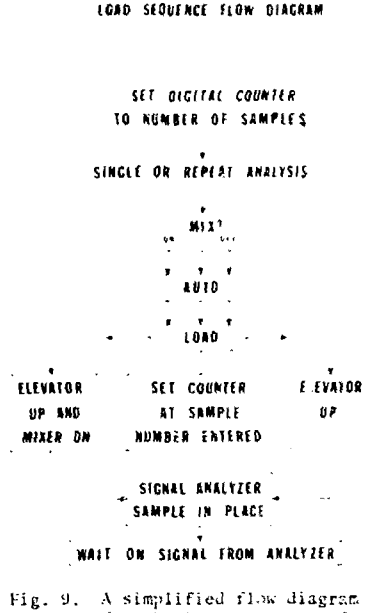

Fig. 9. A simplified flow diagram for the LOAD sequence of the sample changer. The oval boxes indicate operator preselect requirements while the rectangular boxes indicate those operations automatically programmed and which follow depression of LOAD on the primary control panel.

The motor wiring is generally routed through both microswitches and relays. Once an "off" control microswitch is tripped, a relay must provide override control over that microswitch in order to restart the motor (e.g., M2 in the up or down position).

Figure 9 shows a schematic flow diagram of the AUTO logic. The oval boxes indicate the preferred order of initialization steps prior to depressing LOAD on the primary control panel (Fig. 4). The SINGLE or REPEAT analysis switch is located on the secondary control panel (Fig. 6). The rectangular boxes show automatically programmed sequence steps that follow once loading action begins — i.e., sample elevator up. When the pulse-height analyzer returns a logic pulse signalling that data analysis is complete, the flow logic shown in Fig. 10 begins. Following normal sample advance, LOAD returns control to the ELEVATOR UP step shown in the preceding figure.

SUMMARY

An automated sample changer has been developed for fluorescent excitation analysis of selected tracers in biomedical samples. The sample changer contains separately programmed mechanisms driven by

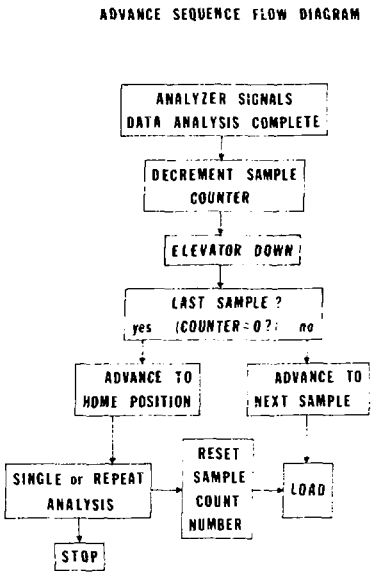

Fig. 10. A simplified flow diagram for the advance sequence of the changer. All these steps follow automatically once the analyzer signals that data analysis is complete.

three small motors coupled with fixed-torque safety clutches. An intermittent motion accurately positions (tolerance ±0.25 mm) a 35-cm-diameter tray which holds 48 2-cc vials. The second mechanism lifts the 2-cc vials about 19 cm into position (tolerance ±0.25 mm) through either a mix or non-mix mode. The mixing mechanism is an integral part of the lift mechanism and tumbles the vials end-over-end four times within 10 cm. This is enough to mix settled, heparinized blood. The lift mechanism clutch shuts off changer power in the event of malfunction or jamming. Safety clutches are set for minimum torque to eliminate hazards to operating personnel. No maintenance of the changer's mechanical parts or bearings is required.

The sample changer is interfaced to an Ultima 2000 programmable pulse-height analyzer which controls the sample changer. The detector is a low-background KeVex spectrometer. The sample changer operates in a manual or automatic mode, and incorporates a digital selection switch which sets the number of samples to be analyzed. A repeat or single-option switch allows a pre-selected number of samples to be counted once, then return to "home" position, there to stop or to be once again analyzed until manually or program stopped. The changer is controlled by relay and integrated circuit sequential logic systems. The changer's control electronics are contained in a Nim-bin which also supplies all of the power needed for the changer. After storage of the pulse-height spectrum in the analyzer for a pre-set time interval, pre-programmed

portions of the spectrum are integrated and through stored calibration constants and equations, the trace element concentrations in the derived units, along with statistical errors and sample ID, are printed out. A logic signal is then returned to the changer calling for the next sample, the analyzer memory is cleared, and the cycle begins again.

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